REMARKS/ARGUMENTS

Applicants wish to thank the Examiner for the telephone interview of February 5, 2009, during which the rejections of claims 1, 2, 4, 5, and 8 were discussed. Specifically, Applicants provided clarification regarding the utility of the animal model of claims 1 and 2, as well as the screening steps of claims 4 and 5. This clarification is reflected in the comments provided below. Claims 4 and 5 have been amended to remove reference to "or suppressing" and to clarify steps involved in the claimed methods of screening as discussed during the telephone interview. No new matter has been introduced by way of these claim amendments.

Claims 1, 2, 4, 5, and 8 are currently pending in the application. Reexamination and reconsideration of the claims are respectfully requested in view of the following remarks. The Examiner's comments in the Office Action dated September 18, 2008 are addressed below in the order set forth therein.

The Rejection of the Claims Under 35 U.S.C. §§101 and 112, First Paragraph, Should Be Withdrawn

The Examiner has maintained the rejections of claims 1, 2, 4, 5, and 8 under 35 U.S.C. §§101 and 112, First Paragraph (enablement). This rejection is traversed for the reasons provided below.

As the basis for the Examiner's rejections, the Examiner states that the usefulness of the mouse of the present invention cannot be found in the screening of TRAM inhibitors. Applicants respectfully submit that a person of ordinary skill in the art would readily understand that the mouse of the present invention and cells thereof play a critical role in the screening of a substance of promoting a response to a ligand recognized by TLR4, as a control of a endotoxin-responsive mouse. Specifically, when the mouse of the present invention and a wild type of the same species are used, and the response to a test substance is compared, if the response is observed only in the wild-type and not in the mouse of the present invention, it can be determined that the test substance specifically stimulates TRAM. On the other hand, if the response is confirmed for both the wild-type and the mouse of the present invention, it can be determined that the test substance is not a substance that specifically stimulates TRAM. If the

mouse of the present invention is not used, it is impossible to evaluate whether the response induced by the test substance is specifically mediated by TRAM or not.

As described above, Applicants have amended claims 4 and 5 to clarify steps involved in the claimed methods of screening using the knock-out mouse of the invention or cells thereof. Accordingly, Applicants request that the Examiner's rejections under 35 U.S.C. §§101 and 112, First Paragraph, be withdrawn.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicants respectfully submit that the rejections of the claims under 35 U.S.C. §§101 and 112, First Paragraph, are overcome. Accordingly, Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited.

It is not believed that extensions of time or fees for net addition of claims are required. However, in the event that extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 C.F.R. §1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

/edward r. ergenzinger/

Edward R. Ergenzinger
Registration No. 49,549

Customer No. 00826
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel Raleigh Office (919) 862-2200
Fax Raleigh Office (919) 862-2260

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